

The status of the do-not-resuscitate order in Chinese clinical trial patients in a cancer centre

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Abstract

Objective—To report and analyse the pattern of end-of-life decision making for terminal Chinese cancer patients.

Design—Retrospective descriptive study.

Setting—A cancer clinical trials unit in a large teaching hospital.

Patients—From April 1992 to August 1997, 177 consecutive deaths of cancer clinical trial patients were studied.

Main measurement—Basic demographic data, patient status at the time of signing a DNR consent, or at the moment of returning home to die are documented, and circumstances surrounding these events evaluated.

Results—DNR orders were written for 64.4% of patients. Patients in pain (odds ratio 0.45, 95%CI 0.22-0.89), especially if requiring opioid analgesia (odds ratio 0.40, 95%CI 0.21-0.77), were factors associated with a higher probability of such an order. Thirty-five patients were taken home to die, a more likely occurrence if the patient was over 75 years (odds ratio 0.12, 95%CI 0.04-0.34), had children (odds ratio 0.14, 95%CI 0.02-0.79), had Taiwanese as a first language (odds ratio 6.74, 95%CI 3.04-14.93), or was unable to intake orally (odds ratio 2.73, 95%CI 1.26-5.92). CPR was performed in 30 patients, none survived to discharge.

Conclusions—DNR orders are instituted in a large proportion of dying Chinese cancer patients in a cancer centre, however, the order is seldom signed by the patient personally. This study also illustrates that as many as 20% of dying patients are taken home to die, in accordance with local custom.

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Keywords: DNR: do not resuscitate; AAD: discharge against advice; CPR: cardiopulmonary resuscitation; end-of-life directives

Introduction

Cardiopulmonary resuscitation (CPR) was first described in 1960; patients were successfully revived by external cardiac massage after experi-

encing cessation in cardiac function.¹ Cardiopulmonary resuscitation has since then been automatically administered to any individual who has experienced abrupt cessation in cardiac or respiratory function,^{2,3} unless otherwise prohibited.

In the 1980s in the USA, CPR was performed in about a third of all hospitalised persons before dying.⁴ After the first CPR, pulse and blood pressure could be established in 30-40% of patients,⁴ although vital signs had to be restored within 30 minutes to be effective,^{5,6} 10-40% survived 24 hours,^{5,7} but only 14-17% lived to hospital discharge,⁷⁻¹⁰ and 11% of patients actually required a second CPR whilst still in hospital.⁸ Fortunately, of those discharged after a successful CPR, more than 90% remained mentally intact.^{5,11}

Analysis has shown that pneumonia, hypotension, renal failure, cancer, sepsis, and a home-bound lifestyle predict for CPR failure with significant in-hospital mortality.^{5,7,10,12,13} Predictors of survival after CPR were formulated from composite evaluation of patient age, diagnoses, mental status, and physical condition, and patients who were unlikely to benefit from CPR counselled against it,^{12,14} guidelines for do-not-resuscitate orders were thus formulated.^{3,7}

The rationale behind a DNR order is threefold: the patient will receive no medical benefit, and at most short-term life prolongation after CPR (a physician-dependent judgment); poor quality of life is expected after CPR, and CPR should also be deferred if there is poor quality of life before cardiopulmonary arrest, the last two dependent on patient standards.¹⁴ The DNR order has the advantage of decreased mechanical ventilation support, decreased traumatic preterminal intervention for the patient, and in general, decreased economic expenses, but an associated higher in-hospital mortality, even after stratification for severity of illness.¹⁵

Once a DNR order is in place there follows the inevitable generalisation of that management

principle to other treatments, which means that auxiliary care available to the patient can be highly variable, since at one extreme it might be seen as necessary to perform all possible treatment up to but excluding CPR, while at the other extreme treatment is limited to comfort measures only.¹⁶ Nevertheless, appropriate institution of nutrition and hydration should never be overlooked.¹⁷⁻¹⁹ With DNR orders being written for 9-20% of all inpatients,¹³⁻¹⁹⁻²² 68-86% of all dying patients,¹⁶⁻²¹ 85-94% of cancer patients,²³ it is obvious they have wide ranging ethical, legal and economic implications.

In the Chinese culture as observed on Taiwan, it is preferable that dying people exhale their last breath at home, signifying a full life, bringing good fortune to future descendants.²⁴ To fulfil that wish, the patient is sometimes intubated to maintain an airway for manual ventilation, regardless of cardiac status, and only extubated at home. This study was designed to report and analyse end-of-life directives of Chinese cancer patients.

Material and methods

This study is a retrospective, descriptive study. Between April 1992, and August 1997, 177 consecutive deaths of patients registered on various clinical trial protocols in our cancer research centre were studied: all patients had detailed medical records, including a detailed account of circumstances surrounding their demise. Patient diagnoses included 56 lung cancers, 46 gastrointestinal cancers, 21 nasopharyngeal cancers, 17 breast cancers, 16 cancers of unknown primary site, and a miscellaneous group of ovarian, cervical cancers, and melanoma.

Informed consent for treatment, as approved by the Veterans General Hospital, Taipei institutional review committee, was obtained from all patients prior to registration for their particular clinical trial, and thus all patients had their diagnosis, treatment, expected therapeutic efficacy, and projected survival formally explained to them in detail, culminating in them signing an informed consent for treatment.

At the point when all active therapy became futile for a particular patient, the family members, but seldom the patient directly, since direct patient communication is not legally required, would be informed of the seriousness of the situation, consulted about communication with the patient, and prompted to make future arrangements, a session usually lasting 15 to 20 minutes. It is important to state that in this group of cancer patients, DNR was discussed with the rationale that CPR would be futile as a result of progressive cancer.¹⁴ However, the patients were seldom given a clear account of

Table 1 Demographic data of 177 Chinese cancer clinical trial patients

Parameter	
Mean age, years (range)	56.5 (19-80)
Male:female ratio	113:64
Marital status, No (%)	
Married	154 (87)
Single	20 (11)
Divorced	3 (2)
Children number, No (%) (single patients excluded)	
0	3 (0-8)
1	7 (4.4)
≥2	18 (12)
Educational level, No (%)	
Illiterate	132 (75)
Literate	21 (12)
Primary school	6 (3.4)
Secondary school	62 (35)
College and beyond	56 (32)
Language, No (%)	
Mandarin	32 (18)
Taiwanese	147 (83)
Diagnosis, No (%)	
Lung cancer	30 (17)
Gastrointestinal cancers (hepatoma, gastric, colon and pancreaticobiliary cancers)	56 (32)
Breast	46 (26)
Nasopharyngeal carcinoma	17 (10)
Metastases of unknown origin	21 (12)
Miscellaneous	16 (9)
Religion, No (%)	21 (12)
Buddhism/Taoism	91 (51)
Christianity	21 (12)
None	65 (36)

their circumstance by the family or friends, and in the overwhelming majority of cases, the medical team was asked to do the same. To our knowledge, none of the patients had made a living will.

Cardiopulmonary resuscitation is defined as application of external chest compressions and rescue breathing.¹ AAD stands for discharge against advice, but in the context of this manuscript, it implies, without exception, that the patient has to be taken to his/her own home to exhale the last breath, a decision that may be patient and/or family directed. DNR means do not resuscitate. The DNR consent form, more correctly, the CPR refusal form, is not considered a legal document in Taiwan, but signing such a form still implies prohibition of external chest compression, intubation and artificial ventilation. In this study, the terms DNR order and the withhold CPR order will be used interchangeably.

Statistical analysis to determine variables important in a patient signing a refusal for CPR, or choosing to conform to custom and die at home, or even insisting upon CPR, was performed by χ -square test with odds ratio for analysis of categorical data, and was considered significant if $p < 0.05$. Survival was calculated by the Kaplan-Meier method with Logrank test.

Table 2 Patient status at the time of signing the DNR consent, and/or the time of choosing to go home to die

Parameter	
Performance status, No (%)	
4	167 (94)
≤3	10 (6)
Pain (common toxicity criteria), No (%)	
Grade 0	45 (25)
Grade 1	5 (3)
Grade 2	28 (16)
Grade 3	37 (21)
Grade 4	62 (35)
Opioid analgesia, No (%)	
None	51 (29)
Codeine	10 (5.6)
Tramadol	5 (3)
Demerol	17 (9.6)
Morphine	94 (53)
Nutritional route, No (%)	
Nil per mouth	85 (48)
Nasogastric feeding	48 (27)
Liquid diet	16 (9)
Soft/bland diet	17 (9)
Regular diet	11 (6)

Results

Patient characteristics are listed in table 1. Our patients ranged in age from 19 to 80 years. Male patients predominated because our cancer unit is affiliated to a veterans hospital. Most were married with children, bachelors were predominantly veterans. Educational level ranged from illiteracy to college and beyond, but well over 80% of patients had received formal education. Religion was Buddhism/Taoism for just over half the patients. Mandarin was the mother tongue for 83% of patients, 17% identified Taiwanese as their first language, a fact with potential influence on the cultural habits that they followed. Financial status was difficult to assess, but treatment was never withdrawn for economic reasons. There has been universal health coverage for all citizens of Taiwan since March 1995, and all patients on clinical trials would be covered for treatment and investigational costs incurred.

Table 2 documents patient status at the time of signing consent to withhold CPR. All patients were in the terminal stage of their disease, with poor performance status. Grade 3 and 4 pain was experienced by 56% of patients, with 75% requiring opioid analgesia. All patients, except those who chose to go home to die, had intravenous access for provision of adequate fluids, nutrition by mouth or via nasogastric tube was not possible in 50% of patients because of poor bowel movements, resulting from peritoneal carcinomatosis or opioid analgesia. The immediate cause of death could be attributed directly to progressive cancer in 95% of patients, with only eight patients dying from sepsis.

Table 3 Details relating to the DNR order and eventual cause of death

Parameter	No (%)
DNR order signed	114 (64.4)
AAD (including 12 patients with a DNR order)	35 (20)
No DNR no CPR	13 (7.3)
CPR performed	30 (17)
DNR (114 patients) signed by	
spouse (husband/wife)	29/35 (56)
children (son/daughter)	17/20 (32)
sibling (brother/sister)	5 (4.4)
Parent	3 (2.6)
Friend	4 (3.5)
Self	1 (0.9)
Duration from diagnosis to death (days)	
DNR patients' mean=774 median=383	
AAD patients' mean=1045 median=390	
CPR patients' mean=590 median=385	
Duration from DNR order to death (days)	114 patients
0-5	76 (66.7)
6-10	15 (13.1)
≥11	23 (20.2)
Duration from AAD to death (days)	35 patients
0	27 (77)
1	5 (14.3)
≥2	3 (8.6)
Cause of death	
disease progression*	164 (93)
sepsis	8 (4.5)
disseminated intravascular coagulation	5 (2.8)

*With resultant organ failure from tumour involvement.

Table 3 documents detailed circumstances at the signing of the DNR order. Consent to forgo CPR was signed for 64.4% of patients, including 12 patients who elected to go home to die. Do Not Resuscitate orders were signed a mean of seven days, and a median of two days preterminal, when the patient was usually incompetent to make any decision, thus only one patient signed for himself, with family members being the signatory in 96.5% of cases. The signatory of the DNR consent being anyone but the patient raises the question of whether the patient surrogate fundamentally reflects the wishes and opinions of the patient, major discrepancies potentially exist.²⁹

Thirty-five patients were discharged against advice, for the purpose of dying at home. The decision to go home to die was made within 24 hours of the patient's demise in more than 90% of cases, therefore, it was necessary to intubate a few patients, with the family maintaining manual ventilation until the patient reached home to exhale the last breath.

In 13 patients who had not signed consent to forgo CPR, resuscitation was not performed because it was judged to be futile by the medical staff. Cardiopulmonary resuscitation was instituted in 30 patients, many of these being at the insistence of the family. To avoid any potential future litigation by the family, CPR was performed for at least 30 minutes. None of the patients lived to hospital discharge.

Table 4 *Factors influencing the signing of DNR consent, and factors influencing the decision to die at home*

Factor	DNR	No DNR	Odds ratio	95% C.I.	AAD	No AAD	Odds ratio	95% C.I.
Age			0.79	0.45–1.53			0.12	0.04–0.34#
<75 years (164 patients)	105	59			34	130		
>75 years (13 patients)	9	4			9	4		
Sex			0.53	0.27–1.02			0.66	0.31–1.41
male (113 patients)	67	46			19	94		
female (64 patients)	47	17			15	49		
Children			0.54	0.24–1.22			0.14	0.02–0.79#
None (27 patients)	14	13			1	26		
≥1 child (150 patients)	100	50			33	117		
Nutritional intake			1.13	0.61–2.10			2.73	1.26–5.92#
No oral intake (85 patients)	56	29			23	62		
Oral intake (92 patients)	58	34			11	81		
Opioid consumption			0.40	0.21–0.77#			0.72	0.30–1.70
None (51 patients)	25	26			8	43		
Opioid (126 patients)	89	37			26	100		
Level of pain			0.45	0.22–0.89#			0.74	0.30–1.84
None (44 patients)	22	22			7	37		
Grade 2–4 (133 patients)	92	41			27	106		
Language			0.80	0.36–1.79			6.74	3.04–14.93#
Taiwanese (30 patients)	18	12			15	15		
Mandarin (147 patients)	96	51			19	128		
Duration of illness			0.83	0.45–1.53			0.93	0.44–1.96
≤1 year (86 patients)	53	33			16	70		
>1 year (91 patients)	60	31			18	73		
Religious affiliation			0.74	0.39–1.39			0.67	0.30–1.50
None (65 patients) vs Buddhism & Christianity (112 patients)	39	26			10	55		
	75	37			24	88		
			1.27	0.68–2.34			1.45	0.68–3.08
Buddhism (91 patients) vs None & Christian (86 patients)	61	30			20	71		
	53	33			14	72		
			1.12	0.43–2.94			0.99	0.13–3.15
Christians (21 patients) vs None & Buddhism (156 patients)	14	7			4	17		
	100	56			30	126		
Survival*								
Median, days	383	360		0.5441	390	374		0.0435

* χ -square test with odds ratio was used for categorical data analysis excluding survival analysis.# $p < 0.05$.

Analysis using the χ -square test shows that a DNR order is more common in patients with pain (odds ratio 0.45, 95%CI 0.22–0.89), especially if requiring opioid analgesia (odds ratio 0.4, 95%CI 0.21–0.89) (table 4).

For patients taken home (AAD patients) to die, age over 75 years (odds ratio 0.12, 95%CI 0.04–0.34), offspring (odds ratio 0.14, 95%CI 0.02–0.79), Taiwanese descent (odds ratio 6.74, 95%CI 3.04–14.93), and inability to intake orally (odds ratio 2.73, 95%CI 1.26–5.92), were all factors significantly influencing the decision to go home.

Conclusion

In this subset of Chinese cancer clinical trial patients, a DNR order was written after signed consent by patient/surrogate in 64.4% of cases. With inclusion of 35 patients (including 12 with DNR orders) who chose to die at home, 82% of patients relinquished active efforts at resuscitation, comparable to the 86–94% DNR rate reported for cancer patients.^{16–23} With better patient understanding of his/her own condition

(diagnosis, treatment, and prognosis), a higher DNR rate would be expected,²⁵ as would a lower rate in non-cancer centre settings.²⁶

It has been reported that as few as 10–33% of patients with DNR orders have been consulted in DNR discussions,^{7–16–27} and other studies show that only 52% of patients not wishing to be resuscitated had DNR orders written.²⁸ In contrast to the 14–87% of patients being involved in signing consent to forgo CPR,^{3–23} only one patient personally signed his own DNR consent in this study, demonstrating that the Chinese patient is often over-protected and precluded from the reality of preterminal circumstances, because of fear of an adverse emotional impact on disease status should the complete truth be revealed.

Discrepancy in patient and health staff preferences also exists.³⁰ In one study, only 50% of physicians correctly predicted end-of-life decisions for their patients.³¹ A structured procedure-specific DNR order sheet certainly helps towards clarifying finer details of the DNR order for the patient, patient surrogate, and health staff.³¹

The DNR consent was signed a mean of seven days, and median of two days preterminal, comparable to the 8.4, and six days recorded for the Memorial Sloan Kettering Cancer Center patients.²³ With such a short interval to death, the DNR consent may well play only a superficial role in averting an unnecessary CPR, without fulfilling the more profound functions of communicating to the patient his/her condition, and promoting patient autonomy by facilitating his/her desire to make arrangements before demise²²; although it is preferable for end-of-life directives to have been made well in advance of signing consent to forgo CPR.

An important factor in the delay in signing the DNR consent lies with the medical staff, who are often reluctant to initiate discussions of CPR and DNR,^{19 27 33} fearing potential adverse effects on patients, who may lose hope in the capacity of doctors to heal them and who may perceive such discussions as filled with foreboding of the worst.²⁴ And this is all in spite of the many surveys that indicate patients are willing and able to take part in such discussions.^{30 31 33 34} Timing of these discussions is tricky, with patients demanding that they occur earlier in the doctor-patient relationship, and at an early stage in the natural course of disease.³⁴ Early communication and discussion is essential between patient, family, religious representative, and hospital staff to clarify patient preferences whilst the patient is still mentally sound; it should also be borne in mind that advance directives evolve over time, and are not fixed by one discussion.³⁵

In the clinical setting, the staff learn to discuss advance directives in an unstructured and haphazard fashion,³⁶ and possibly lack training in the subtleties of obtaining a DNR, and thus often defer the discussion until both patient and family can sense that the situation is grave, and the end is near. Obtaining a DNR may take 20–30 minutes of discussion,³⁷ and the discussion often has to be repeated,³⁷ which poses a burden upon a busy hospital practice. Formal physician education, in the form of workshops, regarding advance directives is urgently needed to improve the frequency, quality, and timing of these discussions.

Do Not Resuscitate orders are more readily assigned to older persons,²⁸ women,¹⁶ those with children acting as surrogate arbitrators,³⁹ patients with functional compromise,²¹ patients with compromised mental status at the time consent is obtained for the DNR order,³⁸ and especially patients who have a cancer diagnosis.⁷ Our analysis finds that severe pain, especially if requiring opioid analgesia, was significantly associated with a DNR order, which would be logical and

humane. Whereas age, patient sex, descendants, nutritional intake, ethnicity, duration of illness or religion were all found to be non-significant (table 4).

Advanced stage cancer patients over 75 years of age, who were unable to take anything orally would be judged to be very ill, and would be more likely to be taken home to die. Having children would encourage the patient to die at home, to pass on good fortune. Taiwanese patients are more likely to be taken home, since the ancestral home of a native mandarin speaker would be so far away as to preclude the trip. In this scenario, patient sex, severity of pain, duration of illness were all found to be insignificant factors.

Cardiopulmonary resuscitation was performed in 17% (30 patients) of cases in this study, slightly higher than the 7.8–13% reported for other centres.^{10 23} The staff, both physicians and nurses, can institute a DNR order without consulting the patient,^{19 27 40} when the physician feels that a CPR is unjustified and futile.⁷ But the patient and/or family can still override this, by demanding CPR, which will be performed to avoid potential future litigation for negligence to treat when required.

In a British study, of 160 cancer patients prospectively followed, 26%, 12%, and 63% died at home, in the hospice or hospital respectively.⁴¹ In the Netherlands, over 40% of terminal patients die at home.²⁶ In Australia, the place of dying has shifted from major metropolitan hospitals to hospice units, with 14% dying at home.⁴² At present in Taiwan, cancer patients prefer to be hospitalised, although 20% of terminal cancer patients choose to exhale their last breath at home, which is very different from being cared for and dying at home. With an increasing number of hospice units established locally, and dissemination of the hospice concept of dying a dignified death, it is hoped that in our society the place of dying will shift from major hospitals to hospice units or even home, and that both patient and medical staff will be more aware of end-of-life decision making and more accepting of earlier advance directives discussions involving the patient personally. It is to be hoped that all of this will contribute to improved management of end-of-life issues.

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